

## REMARKS

At the time of the Office Action, claims 1-38 were pending. Claims 2-38 stand withdrawn as drawn to non-elected subject matter. Claim 1 stands rejected under 35 U.S.C. § 112, second paragraph, as being indefinite. Claim 1 also stands rejected under 35 U.S.C. § 112, first paragraph, for lack of written description and enablement. Claim 1 further stands rejected under 35 U.S.C. § 102(b) for anticipation by Armistead et al. (U.S. Patent 5,978,740), and under 35 U.S.C. § 103(a) as being unpatentable over Armistead et al. (the '740 patent) in view of *In re Gulack* 217 USPQ 401 (Fed. Cir. 1983) and *In re Negai* 70 USPQ2d 1862 (Fed. Cir. 2004). The specification is objected to for the title and for lack of sequence identification numbers. Applicants address each of these rejections and objections as follows.

### Claim Amendments

Claim 1 has been amended to include surrogate “coordinate,” coordinates “encoded on a data-storage medium,” and a program for generating a three-dimensional model “of said Polo-box domain utilizing said coordinates of (i), above.” In addition, new claims 39-44 have been added and claims 14-16, 26, and 37-38 have been cancelled. Support for the amendments to claim 1 and new claims 39-44 is found, for example, on page 7, line 25 to page 8, line 7; page 167, lines 7-10; and claim 1 of the specification as filed.

No new matter has been added by the present amendment. Applicants reserve the right to pursue any cancelled subject matter in this or in a continuing application.

#### Specification/Informalities

The Examiner objects to the specification for the title and for lack of sequence identification numbers. The title of the application has been amended to “Computer Comprising Atomic Coordinates of a Plk-1 Polo-Box Domain and Uses Thereof” (support for this amendment is found for example in claim 1 of the specification as filed).

The specification has been amended to include sequence identification numbers. The objections to the specification can now be withdrawn.

#### Rejections under 35 U.S.C. § 112

##### Written Description

Claim 1 is rejected under 35 U.S.C. § 112, second paragraph, as being indefinite. The Examiner states the recitation of one atomic coordinate from Table 5 for His-538, Lys-540, Trp-414, or Leu-491 is confusing as the data set forth in Table 1 does not disclose positions 414, 491, 538, or 540. Applicants submit that the coordinates corresponding to His-538, Lys-540, Trp-414, and Leu-491 in Table 5 are indicated in the specification. Page 94, lines 26-27 of the specification as filed states:

A summary of statistics for the structure solution and refinement are shown in Table 5. Residues in bold: His538, Lys540, Trp414, and Leu491.

Applicants have clearly indicated which atomic coordinates in Table 5 correspond to His-538, Lys-540, Trp-414, and Leu-491. For these reasons, applicants respectfully request that the rejection of claim 1 under 35 U.S.C. § 112, second paragraph, be withdrawn.

Claim 1 is further rejected under 35 U.S.C. § 112, first paragraph, as being indefinite. The Examiner objects to use of the term “surrogate” as being indefinite. Applicants have amended claim 1 to specify “surrogate coordinate” and have further clarified the meaning of the term “surrogate coordinate” by amending claim 1, item (ii), to recite a program for generating a three-dimensional model “of said Polo-box domain utilizing said coordinates of (i), above.”

Applicants submit that an artisan skilled in the art could easily adjust each of the coordinates from Table 5, in such a way as to conserve the relative relationships between the coordinates (e.g., by rotational or translational modification), resulting in the generation of equivalent three-dimensional structures. Applicants further submit that an artisan skilled in the art of structural biology would understand the term “surrogate coordinate.” In the field of structural biology, it is well known that statistical comparison of two molecular structures first requires a spatial alignment of the molecular coordinates of each structure by a computer software program. Such structural computer software

programs, for example, RasMol or Swiss PDB Viewer, are freely available to the public. Following spatial alignment of the coordinates of two molecular structures, a root mean squared deviation between the coordinates of the two structures can be performed. Thus, an artisan skilled in the art would understand that a set of coordinates from Table 5, each modified to conserve the relative relationships among the coordinates (i.e., “surrogate coordinates”), would generate a three-dimensional model of a Polo-box domain equivalent to the particular model defined by the coordinates of Table 5.

Applicants’ discovery of the three-dimensional structure of the Polo-box domain is not limited to the atomic coordinate data of Table 5, but also, appropriately includes any “surrogate coordinates” that can be used to generate a three-dimensional model of a Polo-box domain having the spatial relationships of the model created directly from the atomic coordinate data of Table 5. As amended, it is apparent from claim 1, item (ii), that use of surrogate coordinates, construed as applicants intend, would result in a three-dimensional model having spatial relationships equivalent to the model of a Polo-box domain derived from the atomic coordinates of Table 5. For these reasons, applicants submit that one skilled in the art would understand the term “surrogate coordinate” and the use of the atomic coordinates of Table 5 for the generation of a three-dimensional model. Applicants respectfully request that the rejection be withdrawn.

Further, the Examiner objects to the broad scope of claim 1, which “requires a computer comprising data of as few as ‘one atomic coordinate’” (see Office Action, page

6). Applicants point out to the Examiner that claim 1, as amended, is directed to “at least one coordinate or surrogate coordinate thereof, from Table 5 *for each* of the following residues: His-538, Lys-540, Trp-414, *and* Leu-491 of a Polo-box domain.” As the computer of claim 1 contains all of the following: one atomic coordinate of His-538, one atomic coordinate of Lys-540, one atomic coordinate of Trp-414, and one atomic coordinate of Leu-491. Thus, as written, claim 1 requires a computer having at least the 4 atomic coordinates (as described above) from Table 5, or surrogate coordinates thereof.

Examiner also objects that the specification fails to disclose a sufficient number of species of the genus of computers of claim 1. Applicants submit that additional examples of computers of the claimed invention need not be provided in the specification, as one skilled in the art would readily understand the genus of computers claimed by the applicants. A skilled artisan in the field of structural biology could easily produce further examples of the genus of computers described by the applicants (e.g., by addition of one or more atomic coordinates from Table 5 to a computer having one coordinate for each of the following residues: His-538, Lys-540, Trp-414, and Leu-491). Thus, applicants submit that the genus of computers claimed are structurally defined by a specific number of atomic coordinates, and hereby respectfully request that rejection of claim 1 under 35 U.S.C. § 112, first paragraph, be withdrawn.

### Enablement

Claim 1 is also rejected under 35 U.S.C. § 112, first paragraph for lack of enablement. Examiner states (page 11) that “in the overly broad scope of the claims, the lack of guidance and working examples provided in the specification, the high level of unpredictability as evidenced by the prior art, and the amount of experimentation required, undue experimentation is necessary for a skilled artisan to make or use the entire scope of the claimed invention.” Applicants respectfully traverse this rejection and discuss the Wands criteria for enablement below.

### *Breadth of the Claims*

Claim 1 to computers having stored therein “at least one coordinate or surrogate coordinate thereof, from Table 5 *for each* of the following residues: His-538, Lys-540, Trp-414, *and* Leu-491 of a Polo-box domain” describes a well-defined genus of computers easily attainable and understood by one skilled in the art given the applicants’ present disclosure (see discussion above).

### *Lack of Guidance and Working Examples*

As is discussed above, applicants submit that additional examples of computers of the claimed invention need not be provided in the specification, as one skilled in the art would readily understand the genus of computers claimed by the applicants. A skilled

artisan in the field of structural biology could easily produce further examples of the genus of computers described by the applicants (e.g., by addition of one or more atomic coordinates from Table 5 to a computer having one coordinate for each of the following residues: His-538, Lys-540, Trp-414, and Leu-491).

*State of the Prior Art, Level of Skill in the Art, and Level of Predictability in the Art*

The level of technological advancement in the field of structural biology is high, such that given the applicants' disclosure, an artisan skilled in the art would easily be able to produce computers of the claimed genus. For example, an artisan would easily be able to add the atomic coordinates of Table 5 to a program such as RasMol or SwissPDB Viewer to produce additional species of the claimed genus of computers.

Examiner also states that at the time of the invention, the level of skill in using the atomic coordinates of a homologous three-dimensional model with an expectation that the model maintains the conformation and activity of a Plk-1 Polo-box domain was low. Examiner cites two references: Lambert et al. (U.S. Patent Application Publication No. 20040137518) and Flower ("Drug Design, Cutting Edge Approaches," Royal Society of Cambridge, Cambridge, UK, 2002). The '518 publication states that "[p]otential or existent homology models cannot provide the necessary degree of specificity" (page 3, paragraph 17). Applicants point out that this statement is taken out of context. In Lambert et al., scientists were attempting to identify specific binding partners of a single

member (i.e., PPAR alpha) of a conserved family of proteins. While the structure of a targeted protein is desired in the particular experiment described in the '518 publication, attainment of such a structure is expensive, time-consuming, and often technically challenging. Homology models are often successfully used in the field of structural biology as a substitute, in the absence of a structure for a particular targeted protein. Applicants further stress that homology models are avored and utilized in many other areas of study and therefore, the three-dimensional model of claim 1, item (ii), can be successfully used by individuals skilled in the art.

In the second cited reference, Flower states “[p]roblems still exist, however: the fitting together of protein domains in a multi-domain protein, the determination of the most likely conformation of protein loops, the correct positioning of amino acid side chains, flexible ligand docking - to name a few” (page 25). Applicants assert that a homology model of the Polo-box domain protein family is not unpredictable and is advantageous for use in the field of structural biology. Applicants point out to the Examiner that the specific residues corresponding to His-538, Lys-540, Trp-414, and Leu-491 of Plk-1 are well-conserved within this family of proteins. Problems regarding the positioning of amino acid side chains are decreased in homology models wherein the amino acid residues are highly conserved. Applicants also note that the atomic coordinates of Table 5 correspond to a single domain and therefore, any problems which



might arise from the fitting together of protein domains in a multi-domain protein are not relevant to the present claim.

Applicants further submit that homology modeling is widely and successfully utilized in the field of structural and molecular biology, further indicating the level of skill and predictability in the field.

*Quantity of Experimentation Needed to Make or Use the Invention*

Applicants assert that given the disclosure of the present invention, one in the field of structural biology would be able to produce and utilize a computer of the present invention. An artisan in the field of structural biology would readily be able to up-load the atomic coordinates of Table 5 to a computer containing a suitable structural software program (e.g., RasMol or Swiss PDB Viewer) and use the structure for experimental purposes. The work required by a skilled artisan to utilize or create different species of the claimed genus of computers is minor and is performed through the modification of computers as described above. What is required once the applicants' coordinates are known is quite literally typing; the experimentation on the part of a skilled artisan is nominal, not undue.

For all the reasons above, applicants submit that claim 1 is enabled by the present specification and respectfully request that the rejection of claim 1 under 35 U.S.C. § 112, first paragraph, for lack of enablement be withdrawn.

#### Rejection under 35 U.S.C. § 102(b)

Claim 1 is rejected under 35 U.S.C. § 102(b) for lack of novelty over Armistead et al. (the '740 patent). The '740 patent teaches the atomic coordinates for a nitrogen atom of a His residue, the atomic coordinates for a nitrogen atom of a Lys residue, the atomic coordinates for a nitrogen atom of a Trp residue, and the atomic coordinates for a nitrogen atom of a Leu residue. The Examiner states that the disclosure of the coordinates above is "considered to be substitutes of 'at least one atomic coordinate of Table 5 for each of H538, K540, W414, and L491" (Office Action, page 13).

Applicants submit that the computer cited in the '740 patent does not contain, as written in claim 1, as amended, "at least one atomic coordinate or surrogate coordinate thereof, from Table 5 *for each* of the following residues: His-538, Lys-540, Trp-414, *and* Leu-491 of a Polo-box domain." The '740 patent clearly fails to disclose one or more coordinates from Table 5 *for each* of the following residues: His-538, Lys-540, Trp-414, and Leu-491. Thus, the applicants respectfully request that rejection of claim 1 under 35 U.S.C. § 102(b) be withdrawn.

#### Rejection under 35 U.S.C. § 103(a)

Claim 1 is rejected under 35 U.S.C. § 103(a) over the '740 patent in view of *In re Gulack* 217 USPQ 401 (Fed. Cir. 1983) and *In re Negai* 70 USPQ2d 1862 (Fed. Cir. 2004). The '740 patent teaches a computer comprising a machine-readable data storage

medium comprising a data storage material encoded with machine-readable data comprising structural coordinates. In *Gulack* and *Ngai*, the courts held that nonfunctional descriptive material in a claim cannot be used to distinguish the claim from the prior art. In view of the references, the Examiner states “there is no evidence of record that the atomic coordinate data of Table 5 imparts functionality to the recited computer when employed as a computer component” (Office Action, page 15).

With regard to computer subject matter, the M.P.E.P. § 2106.01 states:

A claimed computer-readable medium encoded with a data structure defines structural and functional interrelationships between the data structure and the computer software and hardware components which permit the data structure’s functionality to be realized, and is thus statutory.”

Applicants have amended claim 1 to specify “a computer having a memory, wherein said memory has at least one atomic coordinate, or surrogate coordinate thereof, from Table 5 for each of the following residues: His-538, Lys-540, Trp-414, and Leu-491.... encoded on a data-storage medium” (support for the present amendment is found, for example on page 167, lines 7-10, of the specification as filed). Claim 1 has been amended in accordance with M.P.E.P. § 2106.01 as a “data-storage medium” qualifies as a “computer-readable medium.” The amendment of claim 1 clarifies the atomic coordinate data as functional descriptive material to the computer of the claim 1 and

corresponds to the requirement set forth in the M.P.E.P. Thus, applicants respectfully request that the rejection of claim 1 under 35 U.S.C. § 103(a) be withdrawn.

### CONCLUSION

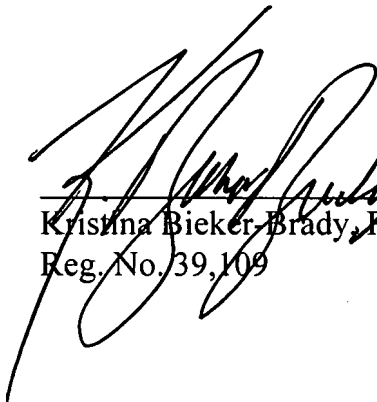
Applicants submit that the application is now in condition for allowance, and such action is hereby requested. Enclosed is a Petition to extend the period for replying to the Office Action for two months, to and including May 7, 2007, as May 6, 2007 is a Sunday, and a check in payment of the required extension fee.

If there are any additional charges or any credits, please apply them to Deposit Account No. 03-2095.

Respectfully submitted,

Date:

May 7, 2007.

  
\_\_\_\_\_  
Kristina Bieker-Brady, Ph.D.  
Reg. No. 39,109

Clark & Elbing LLP  
101 Federal Street  
Boston, MA 02110  
Telephone: 617-428-0200  
Facsimile: 617-428-7045